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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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DEGUZMAN & CARPENTER
P.O.. BOX 50990
Palo Alto, CA 94303

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	5

DATE MAILED: 06/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/052,162	Applicant(s) Crowe et al.
	Examiner Shin-Lin Chen	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 27, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-61* is/are pending in the application.

4a) Of the above, claim(s) *1-15, 37-42, and 50-61* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *16-36 and 43-49* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election of group III, claims 16-36 and 43-49, in Paper No. 4 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.E.P.. § 818.03(a)).

2. Claims 1-15, 37-42 and 50-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 4.

Claims 1-61 are pending and claims 16-36 and 43-49 are under consideration.

Claim Objections

3. Claim 36 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 36 depends on claim 36, i.e. itself, and does not further limit the subject matter of claim 36.

4. Claim 24 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The erythrocytic cells comprising erythrocytic membrane

respectively including those phase transition temperatures does not further limit the erythrocytic cells of claim 16.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 16-34, 36 and 43-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "low phase transition temperature range", "intermediate phase transition temperature range" and "high phase transition temperature range" in claims 16 and 36 is vague and renders the claim indefinite. It is unclear as to the metes and bounds what would be considered "low phase transition temperature range", "intermediate phase transition temperature range" and "high phase transition temperature range". The specification states "The alcohol or sterol reduced erythrocytic cells have a first or low phase transition temperature range greater than about 2°C, an intermediate phase transition temperature range greater than about 20°C, and a high phase transition temperature range greater than about 30°C" (specification, p. 33, lines 13-15). However, the specification fails to specifically define "low phase transition temperature range", "intermediate phase transition temperature range" and "high phase transition temperature range". Further, it appears that there are some overlaps among "low phase transition temperature

range", "intermediate phase transition temperature range" and "high phase transition temperature range", and temperature at 35°C, for example, could be considered "low phase transition temperature range", "intermediate phase transition temperature range" and "high phase transition temperature range". Claims 17-22, 24, 27 and 33 depend on claim 16 but fail to clarify the indefiniteness.

The phrase "erythrocytic cells comprise erythrocytic membrane respectively including said low phase transition temperature range, said intermediate..." in claim 24 is vague and renders the claim indefinite. It is unclear how erythrocytic membranes **can include** phase transition temperature ranges. A phase transition temperature range is the temperature range under which the erythrocytic cells or membranes can have phase transition. But it does not appear that erythrocytic membranes **can include** phase transition temperature ranges.

The phrase "erythrocytic cells selected from a mammalian species and including an alcohol" in claim 43 is vague and renders the claim indefinite. It is unclear how to select erythrocytic cells from **mammalian species and including an alcohol**. It is also unclear what includes an alcohol and whether the alcohol is inside the erythrocytic cells or is in a mixture with the erythrocytic cells provided. Claims 44-49 depend on claim 43 but fail to clarify the indefiniteness. Changing the phrase to "providing mammalian erythrocytic cells having an alcohol" would be remedial.

The phrase "erythrocytic cells having a phase transition temperature range" in claim 16 and the phrase "erythrocytic cells having at least three phase transition temperature ranges" in

claim 43 are vague and render the claims indefinite. It is unclear how erythrocytic cells **can have** phase transition temperature ranges. A phase transition temperature range is the temperature range under which the erythrocytic cells or membranes can have phase transition. But it does not appear that erythrocytic membranes **can have** phase transition temperature ranges. Claims 17-34 depend on claim 16 and claims 44-49 depend on claim 43 but fail to clarify the indefiniteness.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 16-36 and 43-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for loading an oligosaccharide into erythrocytic cells by removing at least a portion of cholesterol from said erythrocytic cells and disposing the erythrocytic cells in an oligosaccharide solution for loading the oligosaccharide into said erythrocytic cells *in vitro*, does not reasonably provide enablement for a process for loading an oligosaccharide into erythrocytic cells by removing at least a portion of **any alcohol** from said erythrocytic cells and disposing the erythrocytic cells in an oligosaccharide solution for loading the oligosaccharide into said erythrocytic cells *in vitro* or *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are directed to a process for loading an oligosaccharide into erythrocytic cells having an alcohol or a process of preparing loaded erythrocytic cells by removing at least a portion of the alcohol from said erythrocytic cells and disposing the erythrocytic cells in an oligosaccharide solution for loading the oligosaccharide into said erythrocytic cells, and the erythrocytic cell composition comprising reduced-alcohol erythrocytic cells produced by said process. Claims 18-21 specify further heating the oligosaccharide solution to increase the loading efficiency of the oligosaccharide into the erythrocytic cells. Claims 23-32 specify the low, intermediate and high phase transition temperature ranges. Claims 33 and 34 specify the oligosaccharide is trehalose.

The claims encompass removing any alcohol from erythrocytic cells. Alcohol is one of a series of organic chemical compounds in which a hydrogen (H) attached to carbon is replaced by a hydroxyl (OH). Alcohol includes methanol, ethanol, propanol, glycerol, ethylene glycol, and fatty alcohol etc. The specification only discloses removing a portion of cholesterol from the erythrocytic cells before loading said cells with oligosaccharide. The specification fails to provide adequate guidance and evidence for removing any type of alcohol other than cholesterol from erythrocytic cells before loading oligosaccharide such that improved loading efficiency of oligosaccharide into erythrocytic cells could be obtained as compared to control erythrocytic cells that no alcohol has been removed from said control erythrocytic cells before loading oligosaccharide *in vitro* or *in vivo*. The specification also fails to provide adequate guidance and evidence for removing cholesterol from erythrocytic cells *in vivo* before loading oligosaccharide

such that improved loading efficiency of oligosaccharide into erythrocytic cells could be obtained *in vivo* as compared to control erythrocytic cells without removing cholesterol from said control erythrocytic cells. There is no evidence of record that removing alcohol other than cholesterol from erythrocytic cells would increase loading efficiency of oligosaccharide into said erythrocytic cells either *in vitro* or *in vivo*. The biological environment *in vivo* is very different from the biological environment *in vitro*. The factors in *in vitro* environment were well controlled, such as the type of medium, the ingredients of the medium, the temperature of the medium and the type of the container used. However, there are various unknown bioactive factors that can not be controlled *in vivo* and these bioactive factors interact with each other and those bioactive factors can interfere with the loading process of oligosaccharide into erythrocyitc cells *in vivo*. The specification fails to provide adequate guidance for how to change the phase transition temperature of erythrocytic cells *in vivo*. In view of the reasons set forth above, one skilled in the art at the time of the invention would not know how to remove alcohol other than cholesterol from erythrocytic cells so as to increase loading efficiency of oligosaccharide into said erythrocytic cells either *in vitro* or *in vivo* or how to practice the claimed invention *in vivo*.

For the reasons discussed above, one skilled in the art at the time of the invention would have to engaged in undue experimentation to practice over the full scope of the invention claimed. This is particularly true given the nature of the invention, the state of the prior art, the breadth of the claims, the amount of experimentation necessary, the working examples provided and scarcity of guidance in the specification, and the unpredictable nature of the art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.